PATENT
Docket No. 252312005706

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Jennifer Bushard

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Stephen M. COUTTS et al.

Serial No.: To be assigned
Continuation of U.S.S.N. 08/769,041

Filing Date: Filed Herewith

For: CONJUGATES OF CHEMICALLY DEFINED NON-POLYMERIC VALENCY PLATFORM MOLECULES AND BIOLOGICALLY ACTIVE MOLECULES (AS AMENDED)

Examiner: To be assigned

Group Art Unit: To be assigned

PRELIMINARY AMENDMENT

Box PATENT APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination of this application on the merits, please enter the amendments below.

AMENDMENTS

In the Title:

Please delete the Title and replace it with --Conjugates of T Cell Epitope Deficient Immunogen Analogs for Humoral Anergy and Chemically Defined Non-Polymeric Valency Platform Molecules--.

In the Cross Reference to Related Applications:

Please delete the entire paragraph on page 1 under the heading "Cross Reference to Related Applications," and substitute therefore the following paragraph:

--This application is a continuation of U.S. Patent Application Serial No. 08/769,041, filed December 18, 1996, which is a divisional of U.S. Patent Application Serial No. 08/453,254, filed May 30, 1995, now U.S. Patent No. 5,606,047, which is a continuation of U.S. Patent Application Serial No. 08/152,506, filed November 15, 1993, now U.S. Patent No. 5,552,391, which is a continuation-in-part of U.S. Patent Application Serial No. 07/914,869 filed July 15, 1992, now U.S. Patent No. 5,276,013; and a continuation-in-part of U.S. Patent Application Serial No. 08/118,055, filed September 8, 1993, U.S. Patent No. 6,060,056. The disclosures of each of these parent applications and patents are incorporated herein by reference.--

In the Specification:

On page 2, line 31, delete "Saski" and insert --Sasaki--;

line 33, delete "(987)" and insert --(1987)--.

On page 3, line 14, delete "fluctuates" and insert --fluctuate--;

line 24, delete "chemical" and insert --synthetic--;

line 29, delete "chemical" and insert --synthetic--.

On page 4, line 30, delete "polyglycol" and insert --polyether--.

On page 5, line 1, delete "$C(CH_2OCH_2CH_2\text{-})_s(OH)_{4\text{-}s}$" and insert --$C(CH_2OCH_2CH_2\text{-})_s(CH_2\ OH)_{4\text{-}s}$--;

line 18, delete "$S(=O)CR^B=CR^B_2$" and replace it with

--$S(=O)_2CR^B=CR^B_2$--;

line 24, delete "-C(=O)CHCHC(=O)-" and insert

---C(=O)CH=CHC(=O)-;

line 25, delete "$S(=O)CR^B=CR^B_2$" and replace it with

--$S(=O)_2CR^B=CR^B_2$--.

On page 10, line 15, delete "chemical" and insert --synthetic--.

On page 12, line 20, delete "$C(CH_2OCH_2CH_2-)_s(OH)_{4-s}$" and insert

--$C(CH_2OCH_2CH_2-)_s(CH_2\ OH)_{4-s}$ --.

On page 13, lines 1 and 10, delete "-C(=O)CHCHC(=O)-" and insert

---C(=O)CH=CHC(=O)-.

On page 15, line 15, after "shown," insert --or with saline--.

On page 17, line 33, after "itself" insert --or when administered as the platform portion of a conjugate--.

On page 19, line 11, after "antibody" insert --and or apoptosis--.

On page 20, line 13, delete "chemical" and insert --synthetic--;

line 17, delete "chemical" and insert --synthetic--.

On page 25, line 10, delete "phosphormidate" and insert --phosphoramidite--.

On page 26, line 12, delete "α-sperm" and insert --sperm--.

On page 27, line 6, delete "eptiopes" and insert --epitopes--.

On page 29, lines 8 and 9, delete "is reacted in the presence of $NaCNBH_3$ with animo platforms to form conjugates" and insert --are reacted with amino platforms in the presence of $NaCNBH_3$ to form conjugates--.

line 11, delete "glycol-lipids" and insert --glycolipids--.

On page 30, line 23, delete "dimethyl formamide" and insert --dimethylformamide--;

line 28, delete "N-methylmorpholine oxide" and insert

--N-methylmorpholine-N-oxide--.

On page 86, line 9, delete "Hydroxysuccinimidyl" and insert --Succinimidyl";

On page 95, line 18, delete "μM" and insert --μmol--.

line 19, delete "μM" and insert --μmol--.

On page 99, line 3, after "synthesis" insert --which incorporates the elements of an acyclic triol moiety (ACT)";

line 7, delete "d-[DMTr-(bzCp(CE)bzA)$_{25}$]" and insert --d-[DMTr-(BzCp(CE)BzA)$_{25}$]--.

On page 100, line 24, after "polynucleotide" insert --,PN-KLH--.

On page 103, line18, before "5' " insert --Tr- --;

line 23, before "5' " insert --Tr- --.

On page 104, line 30, after "nm" insert --,assumed--".

On page 105, line 20, before "5' " insert --Tr- --;

line 23, before "5' " insert --Tr- --.

On page 106, line 23, before "5' " insert --Tr- --;

line 26, before "5' " insert --Tr- --.

On page 119, Table 6, please delete the last entry "8" in the column entitled "Peptide Conjugated" and replace with --9--.

In the claims:

Please cancel claims 2-21 without prejudice or disclaimer.

Please add new claims 22- 51 as follows.

--22. (New) A composition for inducing specific B cell anergy to a T cell dependent immunogen implicated in an antibody-mediated pathology comprising a plurality of a conjugate, wherein said conjugate comprises:

at least two analog molecules of the immunogen conjugated to a chemically defined valency platform molecule, wherein said analog molecules bind specifically to surface antibody on B cells to which the T cell-dependent immunogen binds specifically, and wherein the analog molecules lack T cell epitopes;

wherein the chemically defined valency platform molecule comprises branching groups, and wherein the valency platform molecule contains a specific number of attachment sites whereby the valency of said platform molecule is defined; and

wherein the molecular weight of the valency platform molecules is substantially homogeneous; and

wherein the valency platform molecules have attachment sites at the same location.

23. (New) The composition of claim 22, wherein the branching groups are derived from a functional group selected from the group consisting of diamino acid, triamine, and amino diacid.

24. (New) The composition of claim 22, wherein the analog molecules are the same.

25. (New) The composition of claim 22 comprising conjugates, wherein a said conjugate comprises four analog molecules.

26. (New) The composition of claim 22, wherein the analog molecule is selected from the group consisting of carbohydrates, lipids, lipopolysaccharides, polypeptides, peptides, proteins, glycoproteins, and lipoproteins.

27. (New) The composition of claim 22, wherein the valency platform molecules are substantially non-immunogenic.

28. (New) The composition of claim 22, wherein the analog molecule is a protein.

29. (New) The composition of claim 22, comprising a pharmaceutically acceptable carrier.

30. (New) The composition of claim 29, wherein the composition is suitable for injection.

31. (New) The composition of claim 22, wherein the conjugate comprises polyethylene glycol.

32. (New) The composition of claim 22, wherein the valency platform molecule comprises polyethylene glycol.

33. (New) The composition of claim 22, wherein the conjugate comprises polyethylene glycol having the formula $-CH_2(CH_2OCH_2)_rCH_2-$, wherein r=0 to 300.

34. (New) The composition of claim 22, wherein the valency platform molecule comprises polyethylene glycol having the formula $-CH_2(CH_2OCH_2)_rCH_2-$, wherein r=0 to 300.

35. (New) The composition of claim 22, wherein the valency platform molecule comprises triethylene glycol.

36. (New) The composition of claim 22, wherein the antibody mediated pathology is stroke.

37. (New) The composition of claim 22, wherein the immunogen is an external immunogen.

38. (New) The composition of claim 37, wherein the external immunogen is a biological drug, allergen or a D immunogen associated with Rh hemolytic disease.

39. (New) The composition of claim 22, wherein the immunogen is a self-immunogen.

40. (New) The composition of claim 39, wherein the immunogen is a cardiolipin.

41. (New) The conjugate of claim 39, wherein the self-immunogen is that associated with thyroiditis, diabetes, stroke, male infertility, myasthenia gravis, or rheumatic fever.

42. (New) The composition of claim 22, wherein the immunogen and analog molecules are same chemical class.

43. (New) The composition of claim 42, wherein the immunogen and the analog molecules are polypeptides.

44. (New) The composition of claim 22, wherein the immunogen and the analog molecules are of different chemical classes.

45. (New) The conjugate of claim 22, wherein the antibody-mediated pathology is an autoimmune disorder and the associated immunogen is unidentified.

46. (New) The conjugate of claim 22, wherein the analog molecules are selected from the group consisting of peptides, polypeptides, and proteins.

47. (New) The conjugate of claim 22, wherein the analog molecules are selected from the group consisting of glycoproteins, lipoproteins, carbohydrates, lipids and lipopolysaccharides.

48. (New) A method of inducing specific B cell anergy to a T cell-dependent immunogen in an individual comprising administering to the individual an effective amount of the composition of claim 29.

49. (New) A method of treating an individual for an antibody-mediated pathology in which undesired antibodies are produced in response to a T cell-dependent immunogen comprising administering a therapeutically effective amount of the composition of claim 29 to the individual.

50. (New) A method of making the composition of claim 22, the method comprising forming the conjugates by covalently bonding the analog molecules to the valency platform molecule.

51. (New) A method of making the composition of claim 29, the method comprising combining the conjugates with a pharmaceutically acceptable carrier.

REMARKS

Claims 2-21 have been cancelled, without prejudice or disclaimer of any previously claimed subject matter. New claims 22- 51 have been added. No new matter has been introduced. Support for the new claims is found, for example, on page 3, lines 9-35; page 11, lines 1-19; page 17, lines 19-24; page 19, line 14 - page 20, line 15; pages 26-30; Figures 6A, 6B, 7, and 13; reaction schemes 1-13; and in the originally filed claims.

The specification also has been amended to correct inadvertent typographical errors. In the specification on page 5, a typographical error in the structure of the sulfone, $S(=O)_2$, functionality has been corrected. Support for the amendment appears on page 5, line 18 and lines 25-26, which recite an "α,β-unsaturated sulfone". A sulfone group, as is known in the art, includes two oxygen atoms, and comprises the structure $-S(=O)_2-$.

Applicants request examination of the claims as amended on the merits.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952 referencing docket number 252312005706**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 29, 2000

Respectfully submitted,

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